

ambiguous base; see page 11, lines 38-42, of the specification). Applicants submit herewith a corrected Sequence Listing and diskette including the Sequence Listing in computer readable form.

The Office Action stated that the Notice to Comply had a shortened statutory period for response of one month from the mailing date; however, Applicants never received the Notice. In a telephone conversation with the Examiner on December 9, 1996, the Examiner indicated that it would be permissible to file the new Sequence Listing with this Amendment along with the requisite petition for three months extension of time. Should any other fees be required, Applicants authorize any other fees to be charged to Deposit Account No. 20-1430.

#### The Invention

The Examiner acknowledges that the present invention provides innovative computer-aided methods that are not disclosed or suggested in the prior art for identifying unknown bases in nucleic acids. However, the Examiner rejected the claims under § 101 and § 112, second paragraph. Applicants have amended the claims to overcome the rejections and will discuss each of the Examiner's specific rejections below.

#### The § 101 Rejection

The Examiner rejected claims 60-105 under 35 U.S.C. § 101 as being directed to non-statutory subject matter. More specifically, the Examiner stated that the claims are directed to a computer algorithm which is not applied to physical elements or process steps. Applicants respectfully disagree. The claims recite computer-aided processes which analyze probe intensities indicative of the extent of hybridization of the nucleic acid probes and the sample sequence. The extent of hybridization is indeed a physical quantity just as are electrocardiograph signals (see Arrhythmia Research Tech. v. Corazonix Corp., 958 F2d 1053, 22 USPQ2d 1033 (Fed. Cir. 1992)). In order to more clearly recite the invention, Applicants amended the independent claims to recite that "said computer system generat[es] a base call"

that identifies an unknown base. Therefore, the claims recite statutory computer-aided processes of receiving probe intensities indicative of hybridization with a sample sequence and generating a base call of an unknown base in the sample sequence.

The Examiner suggested that the claims "should be amended so that if viewed without the algorithm the process would stand alone." Applicants understand the Examiner to say that the claims should recite statutory subject matter in the abstract, without consideration of an algorithm or computer. For example, processes of curing synthetic rubber are statutory subject matter so a process of curing synthetic rubber that utilizes a computer is also statutory subject matter (see Diamond v. Diehr, 450 US 175, 209 USPQ 1 (1981)). Applicants submit that processes for identifying unknown bases in sample nucleic acids are statutory subject matter so the recited computer-aided processes are also statutory subject matter.

Applicants have reviewed the Examination Guidelines for Computer-Related Inventions in § 2106 of the MPEP (see, e.g., the section entitled "Manipulation of Data Representing Physical Objects or Activities" in MPEP § 2106(IV)(B)(2)(b)(i)). Applicants fully believe that the pending claims are directed to statutory subject matter. Applicants invite the Examiner to telephone the undersigned if a telephone discussion would facilitate prosecution of the subject application.

The § 112, Second Paragraph, Rejections

The Examiner rejected claims 60-105 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject invention. With regard to claim 60, the Examiner indicated it is not clear to what the probe intensities are compared. Applicants amended claim 60 to recited that the probe intensities are compared to each other (see, e.g., Figs. 3, 4A and 5A). Accordingly, the rejection is overcome.

Additionally, the Examiner stated that claim 60 is indefinite in that it is not clear how one extrapolates from "comparing" to "identifying." Applicants respectfully submit

that, when read in light of the specification as the case law requires, the claims are not unclear. Applicants' specification provides full detail on possible "comparing" and "generating" (as amended) steps. For example, the highest probe intensity may be compared to the next highest probe intensity to generate a ratio. If this ratio is greater than a predetermined ratio cutoff, the unknown base will be called according to (e.g., complementary to) a base in the probe with the highest intensity (see page 14, lines 23-34). Many of the dependent claims recite further details on these steps (see, e.g., claims 61-63). As Applicants' specification provides ample description of exemplary ways that the present invention may be performed, Applicants request that this rejection be withdrawn.

With regard to claim 64, the Examiner indicated it is unclear how the probe intensities are sorted. Applicants amended claim 64 to recite that the probe intensities are sorted "by intensity" (see, e.g., page 14, line 17). Accordingly, the rejection is overcome.

The Examiner indicated that in claim 70 it is unclear what characteristic of the probe "identifies" the unknown base. As described in the specification, the nucleic acid probes are generally complementary to the sample sequence in order to allow for hybridization between the probes and the sample sequence. Applicants amended claim 70 to recite that the unknown base is identified according to "a base" of a probe with a highest ratio (see page 24, lines 5-10). Accordingly, the rejection is overcome.

The Examiner rejected claims 72 and 94. In a sincere effort to expedite prosecution. Applicants canceled these claims rendering the rejections moot.

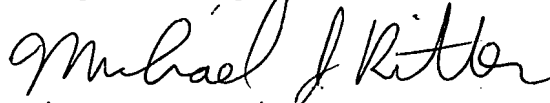
The Examiner rejected claims 81, 83, and 92 for the same reasons as claims discussed above. Applicants amended these and other claims in the manner discussed to overcome the rejections. Therefore, Applicants have addressed all the § 112, second paragraph, rejections and respectfully request that these rejections be withdrawn.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at (415) 326-2400.

Respectfully submitted,



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